REMARKS

Reconsideration of this application is respectfully requested. Claim 23 has been amended. This amendment adds no new matter.

Rejections under 35 U.S.C. § 112, first paragraph

Claims 23-39 were rejected under 35 U.S.C. § 112, first paragraph as allegedly not being enabled for a method of introducing a site directed double-strand break in DNA of a cell *in vivo*. Applicants traverse the rejection.

The Examiner based the rejection on publications discussing the difficulties with gene therapy generally. In contrast to the papers cited by the Examiner, applicants' method does not require long-term expression of a transgene. Rather, in applicants' claimed method, expression of the endonuclease can be transient to create a double-stranded break. Accordingly, the problems suggested by the Examiner are not relevant to applicants' claimed method.

Nevertheless, claims 23-39 have been amended to recite that the cell is "isolated." According to the Examiner: "Claims drawn to an isolated host cell would obviate the instant rejection." (Office Action at 5.) Accordingly, applicants request withdrawal of the rejection.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 23-39 were rejected under 35 U.S.C. § 112, second paragraph as allegedly being indefinite. The Office contends that it is not clear how the endonuclease is provided to the cell in applicants' claims.

Applicants traverse the rejection. Applicants' specification teaches various methods of how an endonuclease can be provided to a cell:

> The gene can be expressed under inducible or constitutive promoter of the retrovirus or of a cellular gene, or by gene trap after homologous recombination.
>
> A variety of plasmids containing I-*Sce* I producing the endonuclease can be constructed. Expression vectors such as pCMVI-SceI(+) or similar constructs containing the ORF, can be introduced in cells by transient transfection, electroporation or lipofection. The protein can also be introduced directly into the cell by injection of liposomes.

(Specification at 83-84.) In view of the teachings of the specification, the skilled artisan would understand that providing an endonuclease to a cell could be achieved by numerous methods.

Nevertheless, to expedite prosecution, applicants have amended claim 23 to recite that the Group I intron encoded endonuclease is provided to the cell "by genetically modifying the cell with a nucleic acid comprising said Group I intron encoded endonuclease or by introducing said Group I intron encoded endonuclease protein into the cell." Accordingly, applicants submit that claims 23-39 are definite and respectfully request withdrawal of the rejection.

Obviousness-type double-patenting rejections

Claims 23-39 were rejected under the judicially created doctrine of obviousness-type double-patenting over claims 1-27 of U.S. Patent 6,610,545 B2; claims 1-7 of U.S. Patent 6,238,924 B1; claims 27-29 of U.S. Patent 5,962,327; and claims 1-17 of U.S. Patent 5,792,632. Claims 23-39 were *provisionally* rejected under the judicially created

doctrine of obviousness-type double-patenting over claims 31-50 of copending Application No. 10/152,994 and claims 24-40 of copending Application No. 10/931,246.

Solely to expedite prosecution of this application and not in acquiescence to this rejection, applicants submit herewith Terminal Disclaimers over U.S. Patent Nos. 6,610,545; 6,238,924; 5,962,327; and 5,792,632, and U.S. Application Nos. 10/152,994 and 10/931,246 in accordance with 37 C.F.R § 1.321(c). Accordingly, applicants respectfully request withdrawal of these rejections.

Applicants respectfully submit that this application is in condition for allowance. In the event that the Examiner disagrees, he is invited to call the undersigned to discuss any outstanding issues remaining in this application in order to expedite prosecution.

Please grant any extensions of time required to enter this paper and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

Dated: February 13, 2007

By: _____

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